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Applicant : Robert J. Winchester, et al.

Serial No.: 09/500,746

Filed : February 9, 2000

For  USES OF INHIBITORS FOR THE ACTIVATION OF CXCR4
RECEPTOR BY SDF-1 IN TREATING RHEUMATOID
ARTHRITIS

1185 Avenue of the Americas
New York, New York 10036
November 30, 2000

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with his duty under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed below and on the accompanying PTO Form 1449 attached hereto as **Exhibit A** and the International Search Report attached hereto as **Exhibit B**. Copies of these Documents are attached hereto as **Exhibit C-S**.

1. U.S. 5,563,048 (Honjo et al.) October 8, 1996 (**Exhibit C**);
2. Bleul C.C., Fuhlbrigg R.C., Casasnovas J.M., Aiuti A., Springer T.A., A Highly Efficacious Lymphocyte Chemoattractant, Stromal Cell-Derived Factor 1 (SDF-1), J. Exp. Med. (1996) 184:1101-9 (**Exhibit D**);
3. Bombara, M.P., et al., Cell Contact Between T Cells And Synovial Fibroblasts Causes Induction Of Adhesion Molecules And Cytokines, J. Leukoc. Biol. (1993) 54(5):399-406 (**Exhibit E**);
4. Delgado, E., et al., Mature Dendritic Cells Respond To SDF-1, But Not To Several Beta Chemokines, Immunobiology (1998) 198:490-500 (**Exhibit F**);

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5. Dinant, H.J. and Dijkmans, B.A., *New Therapeutic Targets For Rheumoid Arthritis*, *Pharm. World. Sci.* (1999) Apr. (Exhibit G);
6. D'Apuzzo M., Rolink A., Loetscher M., Hoxie J.A., Clark-Lewis I., Melchers F., et al., *The Chemokine SDF-1, Stromal Cell-Derived Factor 1, Attracts Early Stage B Cell Precursors Via The Chemokine Receptor CXCR4*, *Eur. J. Immunol.* (1997). 27:1788-1793 (Exhibit H);
7. Goddard D.H., Grossman S.L., Moore M.E., *Autocrine Regulation Of Rheumatoid Arthritis Synovial Cell Growth in vitro*, *Cytokine* (1990) 2:149-155 (Exhibit I);
8. Iacobelli S., Arno E., D'Orazio A., Coletti G., *Detection Of Antigen Recognized By A Novel Monoclonal Antibody In Tissue And Serum From Patients With Breast Cancer*, *Cancer Res.* (1986) 46(6):3005-3010 (Exhibit J);
9. Nagasawa T., Hirota S., Tachibana K., Takakura N., Nishikawa S., Kitamura Y., et al., *Defects Of B-Cell Lymphopoiesis And Bone-Marrow Myelopoiesis In Mice Lacking The CXC Chemokine PBSF/SDF-1*, *Nature* (1996) 382:635-8 (Exhibit K);
10. Ponteziere C., Desmoulins D., Ageray J., Ekindjian O.G., Cals M.J., *Comparative Proliferation Of Non-Rheumatoid Human Synovial Cells*, *Int. J. Tissue React.* (1990) 12(4):229-236 (Exhibit L);
11. Ritchlin C.T., Dwyer E., Bucala R., Winchester R., *Sustained And Distinctive Patterns Of Gene Activation In Synovial Fibroblasts And Whole Synovial Tissue Obtained*

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*From Inflammatory Synovitis, Scand. J. Immunol. (1994)
40(3):292-8 (Exhibit M);*

12. *Ritchlin C.T., Winchester R.J., Potential Mechanisms For Coordinate Gene Activation In The Rheumatoid Synoviocyte: Implications And Hypotheses, Springer Semin. Immunopathol. (1989) 11:219-234 (Exhibit N);*
13. *Schols et al., Bicyclams, A Class Of Potent Anti-HIV Agents, Are Targeted At The HIV Coreceptor Fusin/CXCR-4, Antiviral Research (1997) 35:147-156 (Exhibit O);*
14. *Shirozu M., Nakano T., Inazawa J., Tashiro K., Tada H., Shinohara T., et al., Structure And Chromosomal Localization Of The Human Stromal Cell-Derived Factor 1 (SDF-1) Gene, Genomics (1995) 28(3):495-500 (Exhibit P);*
15. *Smith C.A., Properties Of Synovial Cells In Culture, J. Exp. Med. (1971) 134(3):306s-312s (Exhibit Q);*
16. *Winchester, R., F. Su, and C. Ritchlin, Alteration Of Synoviocytes By Inflammation- The Source OF A Persistent Non-Immunologic Drive In Synovitis: Analysis Of Levels Of MRNA Expression By A Simple Multi-Gene Assay, Clin. Exp. Rheumatol. (1993) 11 Suppl 8:S87-90 (Exhibit R);*
17. *Zou, Y.R., et al., Function Of The Chemokine Receptor CXCR4 In Haematopoiesis And In Cerebellar Development, Nature (1998) 393(6685):595-9 (Exhibit S);*

Applicants request that the Examiner make these documents of record in the subject application.

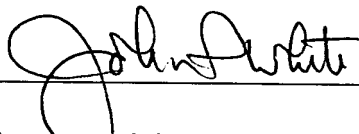
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Applicants maintain that none of the above listed documents which are citable as a reference against the subject application disclose or suggest the invention now being claimed. Applicants attach hereto as Exhibits C-S copies of the above-listed references. Applicants request that the Examiner make these documents of record.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such additional fee to Deposit Account No. 03-3125.


Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents,
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Date
11/30/00